Pregnancy &Glomeruler Disease

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Happy Family

Healthy Pregnancy

Falling birth rate: Demographic transition or disaster?

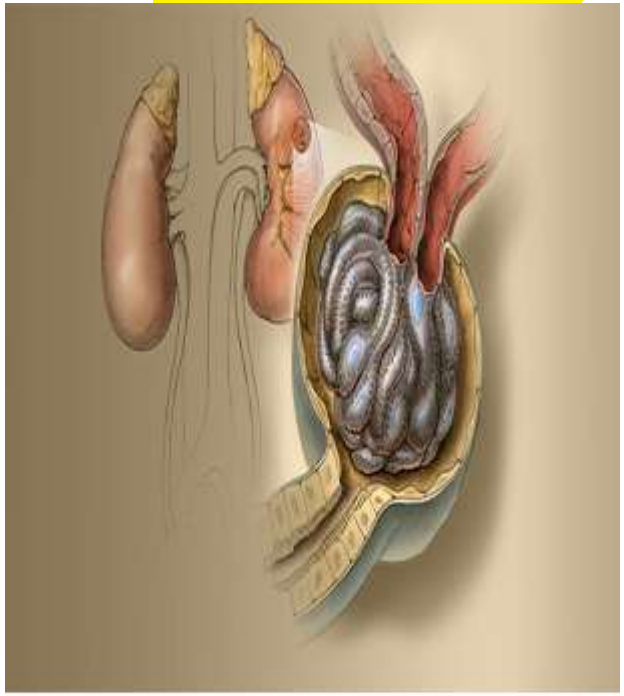
- 131.4 million births per year
- 360,000 births per day
- 15,000 births each hour
- 250 births each minute
- **4 births each second of every day**

Physiological process with possible serious complications

The Whole Family Suffers

Challinging Situation

Pregnancy

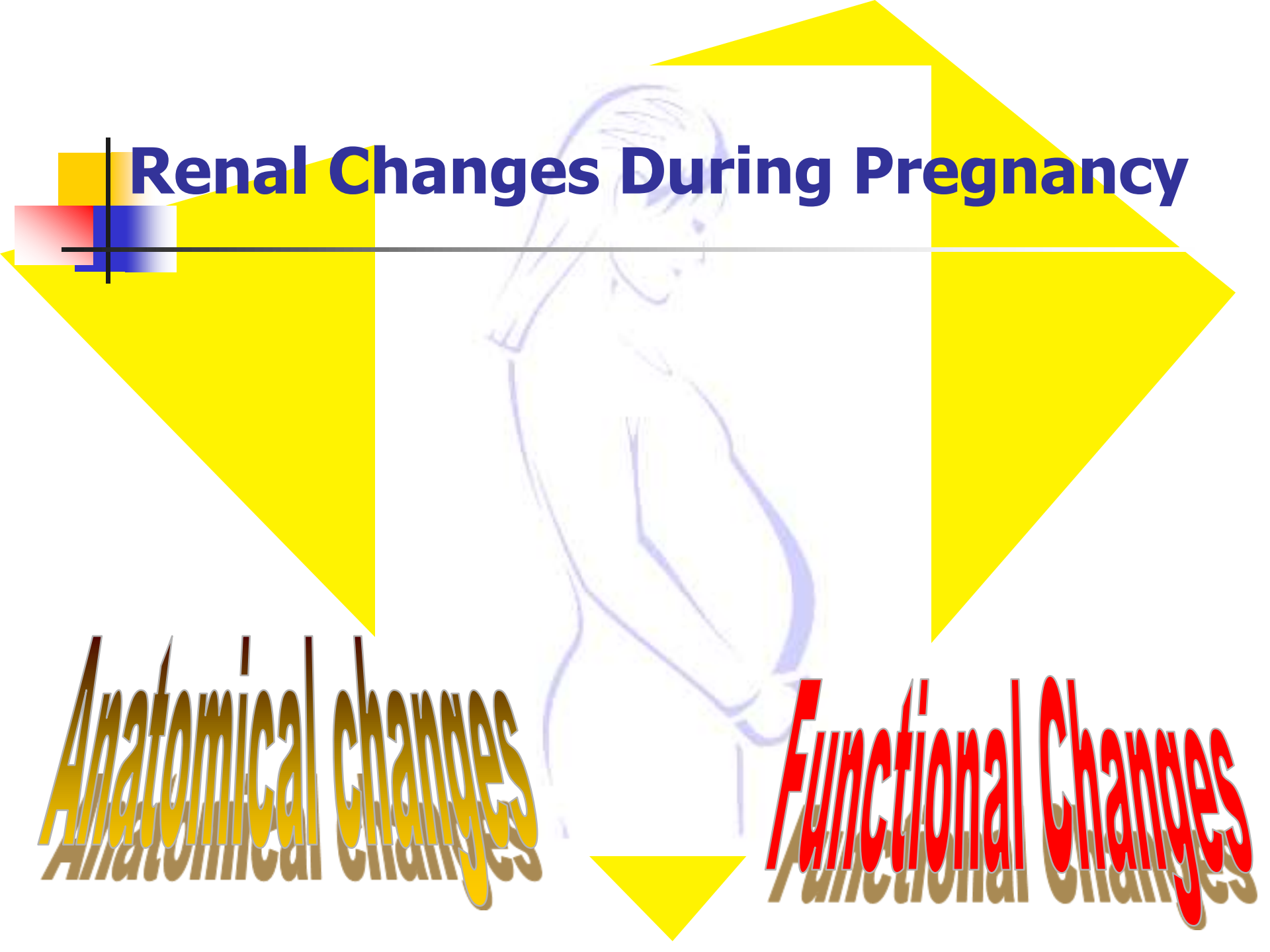


Agenda

- What is the **physiolgy** of normal pregnancy?
- Does Pregnancy **Induce** a glomeruler injury ?
- What is the **Effect** of pregnancy on glomeruler diseases ?
- What is the **Outcome** of pregnancy in the context of glomeruler disease ?
- What are the **Recommendations** ?

Physiological review

Renal Changes During Pregnancy

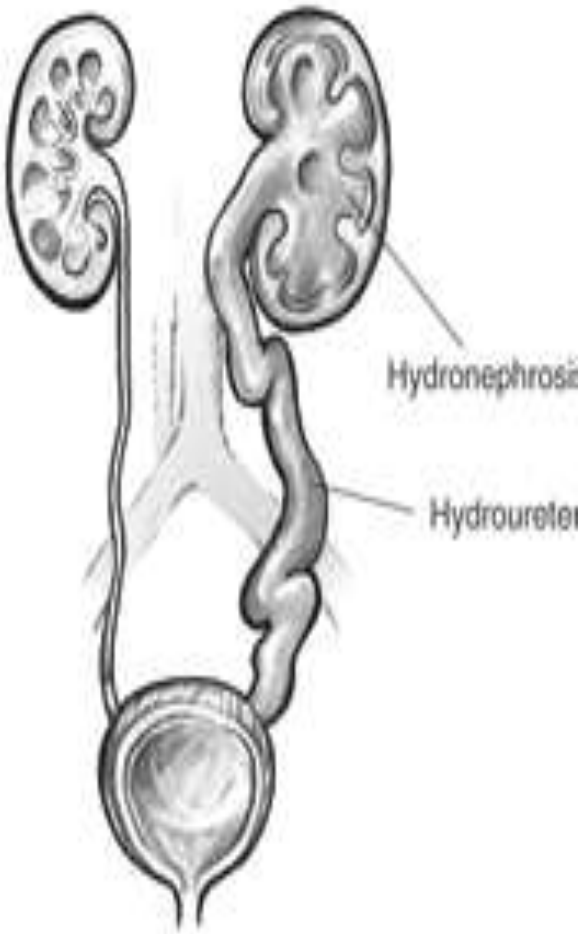


Anatomical changes

Functional Changes

Physiology Review

Anatomical changes



Gynecol Obstet Invest 2012;74:274–281

Hydronephrosis in normal pregnancy. Intravenous urogram at 36 weeks' gestation.

Comprehensive Clinical Nephrology, 4th ed,41,498(2010)

Physiology Review

Heamodynamic and Glomeruler filtration changes

↑ COP
↓ Sytemic vascular resistance
↓ Mean arterial pressure

↑RPF &GFR
↓ plasma osmolality and serum Na

Functional Changes

Gynecol Obstet Invest 2012;74:274–281

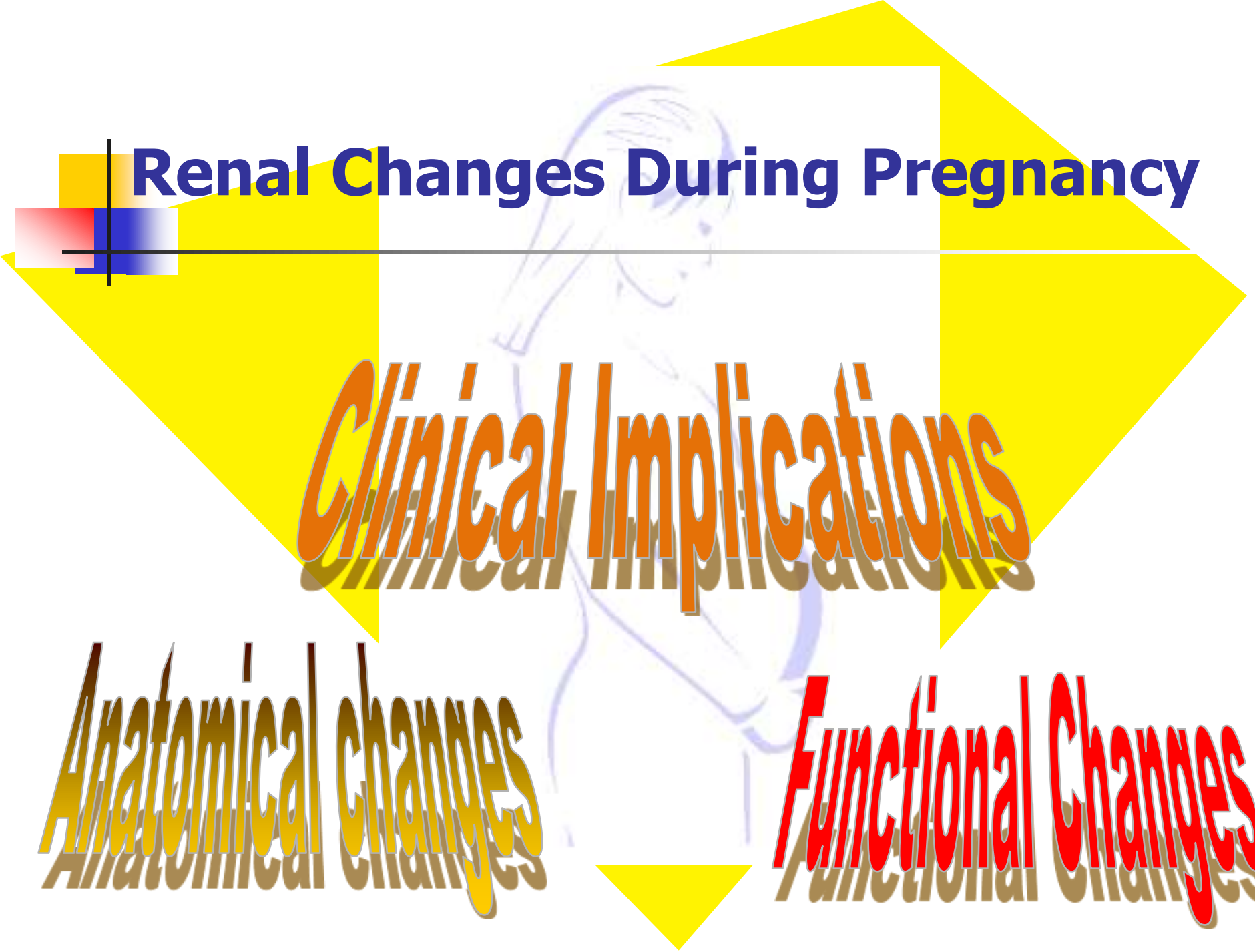
Renal Changes During Pregnancy

Changes in Some Common Indices During Pregnancy		
	Nonpregnant	Pregnant
Hematocrit (%)	41	33
Plasma protein (g/dl)	7.0	6.0
Plasma osmolality (mOsm/kg)	285	275
Plasma sodium (mmol/l)	140	135
Plasma creatinine (mg/dl, µmol/l)	0.8 (73)	0.5 (45)
Blood urea nitrogen (mg/dl)	12.7	9.3
Plasma urea (mmol/l)	4.5	3.3
pH units	7.40	7.44
Arterial PCO_2 (mm Hg)	40	30
Plasma bicarbonate (mmol/l)	25	20
Plasma uric acid (mg/dl, µmol/l)	4.0 (240)	3.2 (190) early 4.3 (260) late
Systolic BP (mm Hg)	115	105
Diastolic BP (mm Hg)	70	60

Functional Changes

Comprehensive Clinical Nephrology, 4th ed,41,567(2010)

Renal Changes During Pregnancy



Clinical Implications

Urinary frequency

Incontinence

Nocturia

Dependent edema

Clinical Implications

After Delivery

Anatomical changes

Functional Changes

Glomeruler disease and pregnancy

- Denovo Pregnancy Related
- Denovo Pregnancy Unrelated
- Preexisting

Does Prenancy induce a glomeruler injury ?

PATHOPHYSIOLOGY of the RENAL BIOPSY

www.jasn.org

The Glomerular Injury of Preeclampsia

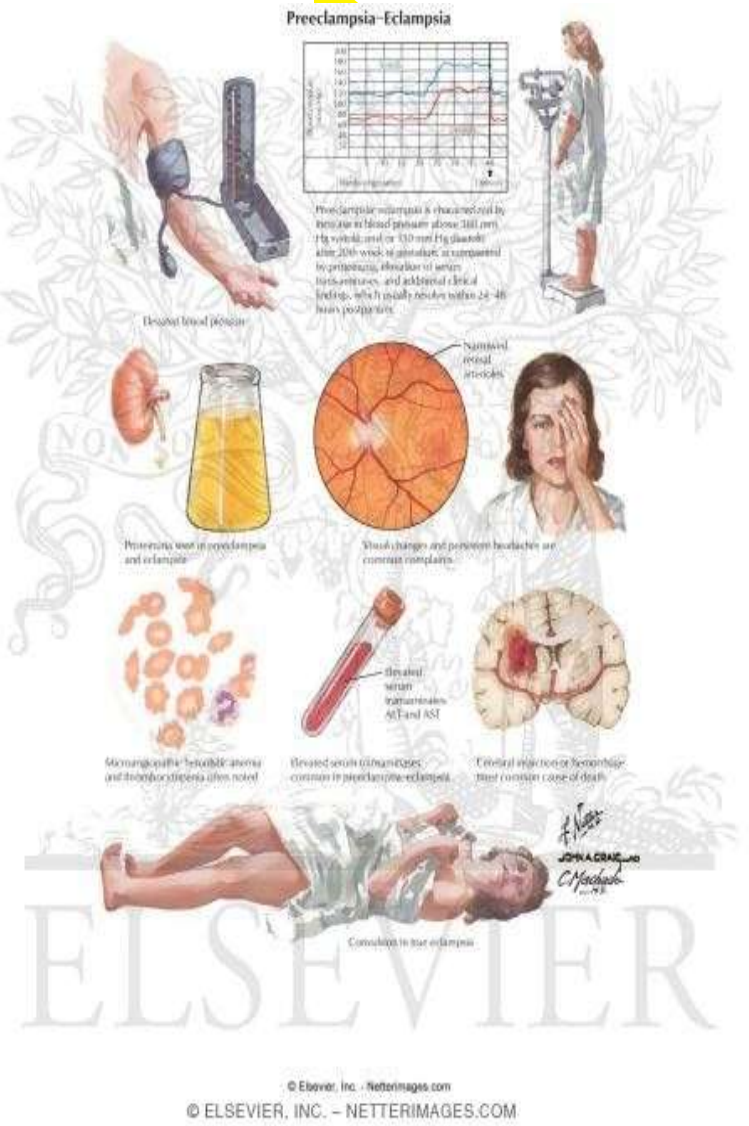
Isaac E. Stillman*† and S. Ananth Karumanchi†‡

*Department of Pathology and Renal Division, Department of Medicine, and ‡Renal, Vascular and Molecular Medicine Divisions, Departments of Medicine, Obstetrics & Gynecology, Beth Israel Deaconess Medical Center, and †Harvard Medical School, Boston, Massachusetts

J Am Soc Nephrol 18: 2281–2284, 2007.

preeclampsia

Preeclampsia (PE) is a pregnancy-specific and multisystemic disorder characterized by the onset of high blood pressure and proteinuria which develop after 20th week of gestation.



Gynecol Obstet Invest 74:274–281 (2012)

first to use the term, “eclampsia”, a Greek word meaning “lightning”, perhaps it refers to a sudden and unexpected convulsions that may arise in the pregnant ladies.

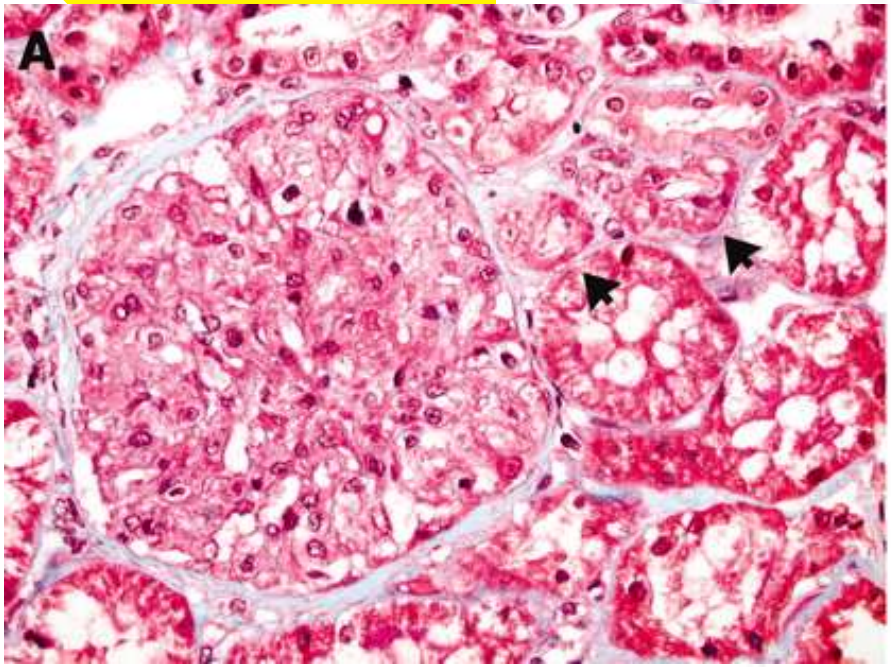
ISSN 1085-6862, 2013

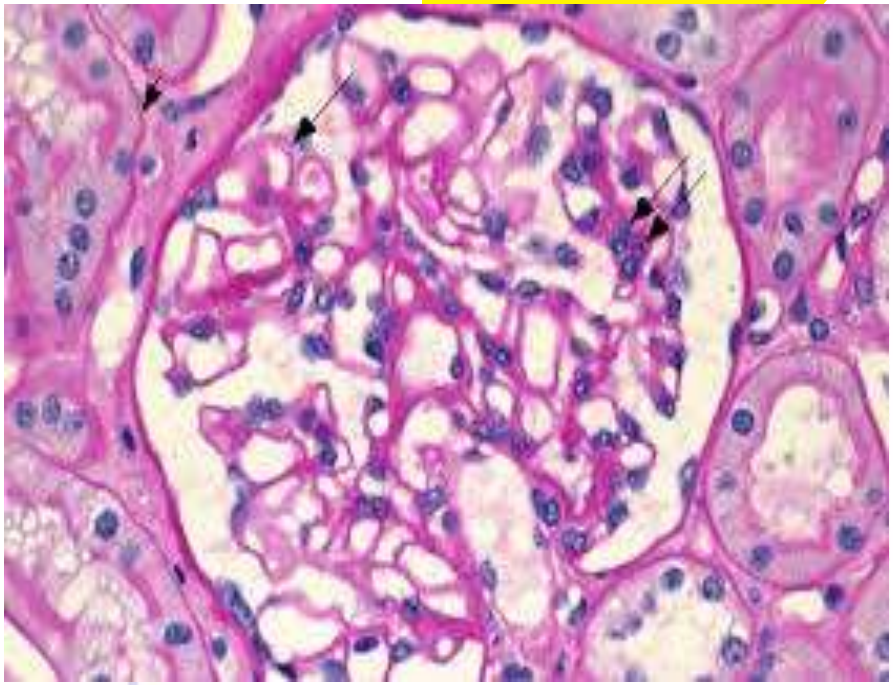
preeclampsia

- preeclampsia complicate up to 8% of pregnancies.
- The most frequent renal complication of pregnancy
- So, some authors considere it as the ***most common glomerular*** disease worldwide .

Nephrol Dial Transplant 27 (Supple 3): iii51–iii57 (2012)

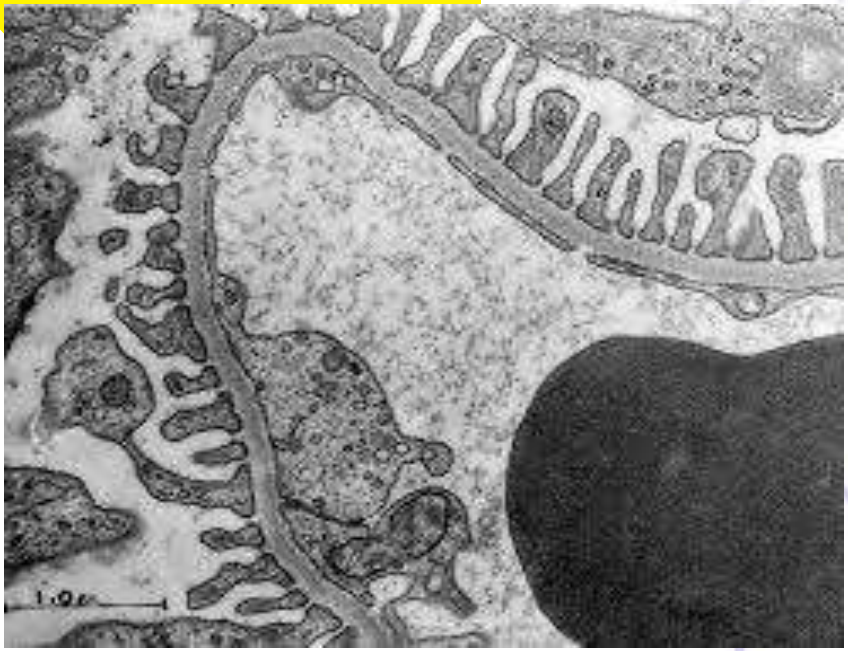
Glomeruler endotheliosis ***LM***

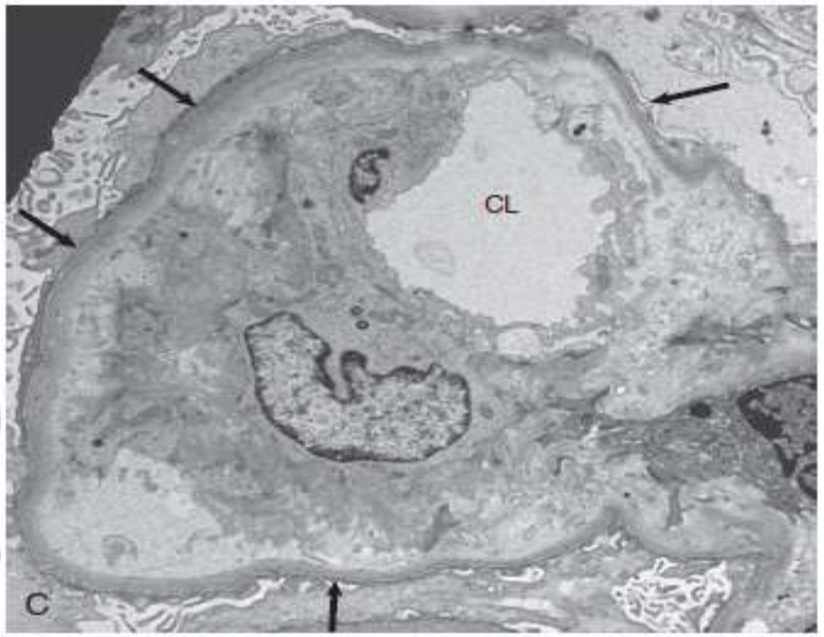




J Am Soc Nephrol 18: 2281–2284, 2007.

Glomeruler endotheliosis *EM*





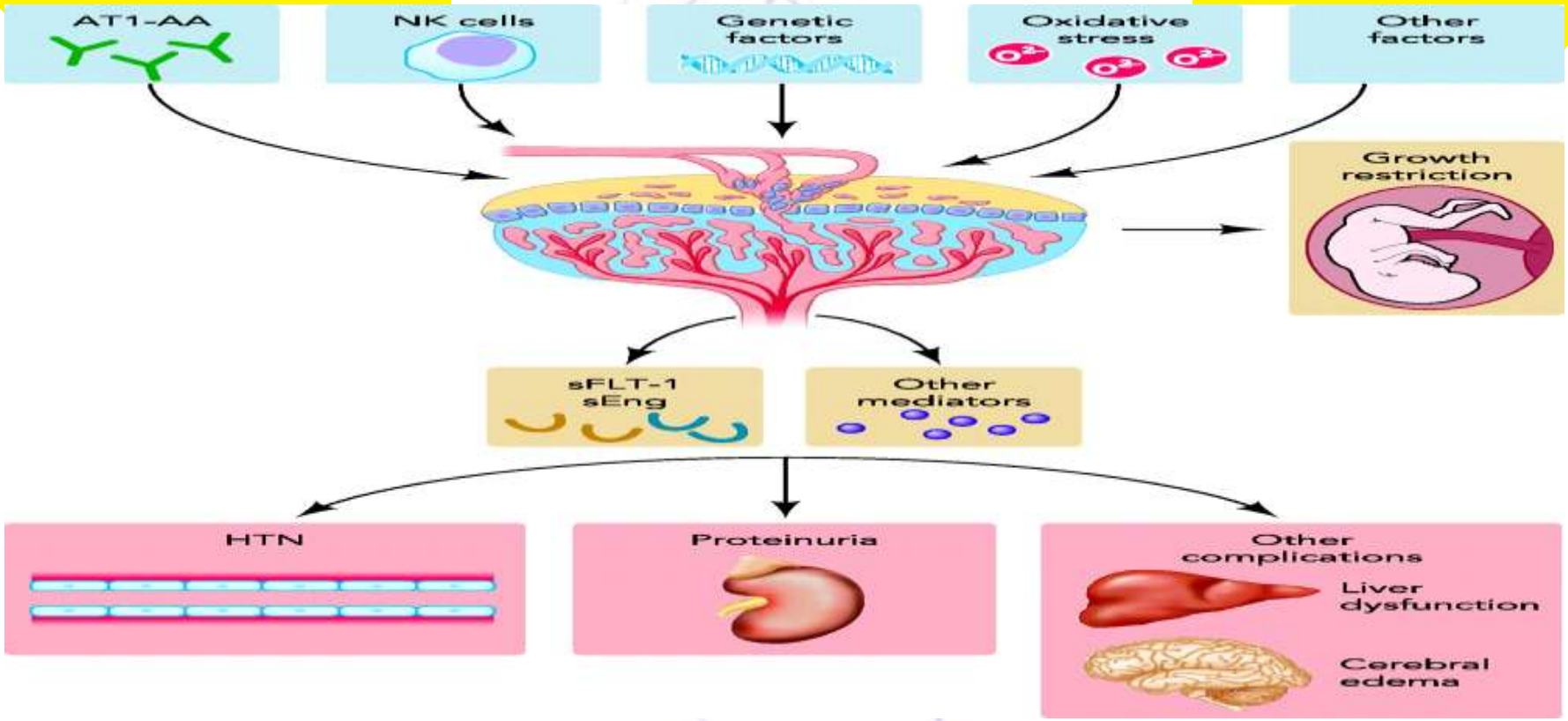
J Am Soc Nephrol 18: 2281–2284, 2007.

Pathogenesis

- One of the great mysteries in the field of OB.

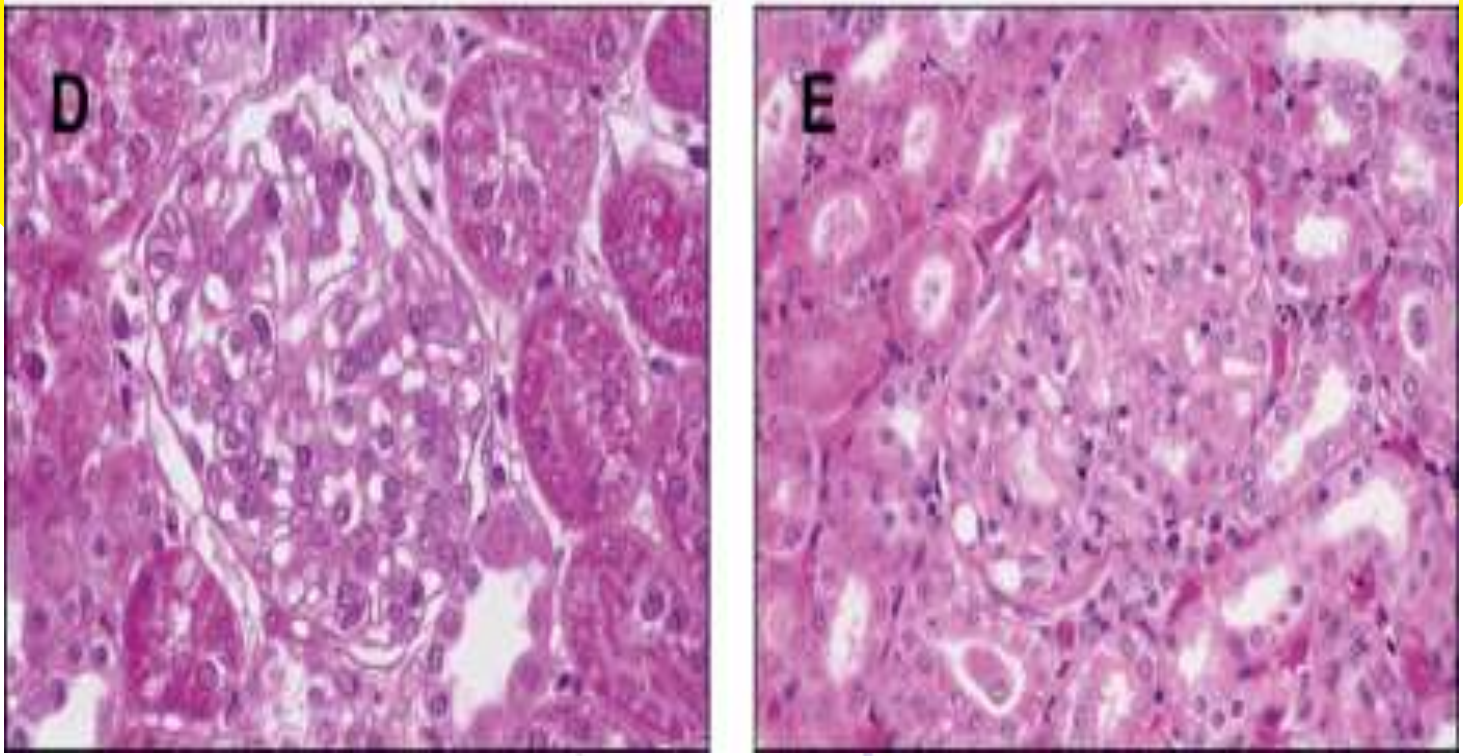
- It is still labeled a "disease of theories".

Abnormal placentation



Circulation 2011; 123:2856-2869

Rat glomeruler endotheliosis



Kidney International vol 7,pp 2101-2113, (2005

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BJOG: an International Journal of Obstetrics and Gynaecology
September 2003, Vol. 110, pp. 831–836

Glomerular endotheliosis in normal pregnancy and pre-eclampsia

Helena Strevens[a,*], Dag Wide-Swensson[a], Alastair Hansen[b], Thomas Horn[b], Ingemar Ingemarsson[a], Svend Larsen[b], Julian Willner[c], Steen Olsen[b]

BJOG: an International Journal of Obstetrics and Gynaecology
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Table 2. Light microscopy; degree of endotheliosis. Fischer's exact test reveals significant differences between women with proteinuric hypertension and controls ($P < 0.00001$), women with non-proteinuric hypertension and controls ($P = 0.02$) and between the two hypertensive groups ($P = 0.01$).

Semiquantified score	Healthy controls ($n = 12$)	Hypertensive women ($n = 35$)	
		Non-proteinuric hypertension ($n = 8$)	Proteinuric hypertension ($n = 27$)
0	7	0	0
1	4	4	1
2	1	2	12
3	0	2	14

Pre-eclampsia may be the extreme of the adaptational process to normal pregnancy, rather than a separate abnormal condition

Case report

AJKD
AMERICAN JOURNAL OF KIDNEY DISEASES

Steroid-Responsive Idiopathic Glomerular Capillary Endotheliosis: Case Report and Literature Review

Idiopathic glomerular capillary endotheliosis

may be a newly recognized glomeruler entity potentially responsive to steroid and cytotoxic regimens.

American Journal of Kidney Diseases , volume 45,issue 6(2005)

Fate of preeclampsia

Pre-eclampsia → later CKD

CMAJ RESEARCH

Association between hypertensive disorders during pregnancy and end-stage renal disease: a population-based study

I-Kuan Wang MD, Chih-Hsin Muo MS, Yi-Chih Chang PhD, Chih-Chia Liang MD, Chiz-Tzung Chang MD PhD, Shih-Yi Lin MD, Tzung-Hai Yen MD PhD, Feng-Rong Chuang MD, Pei-Chun Chen PhD, Chiu-Ching Huang MD, Chi-Pang Wen MD PhD, Fung-Chang Sung PhD, Donald E. Morisky ScD

See related commentary by Spaan and Brown on page 199 and at www.cmaj.ca/lookup/doi/10.1503/cmaj.130007

ABSTRACT

Background: Studies into the association between hypertensive disorders during pregnancy and end-stage renal disease are limited. We investigated the risk of end-stage renal disease after delivery among women with hypertensive disorders during pregnancy.

Methods: We used insurance claims data from 1998 to 2009 to identify 26 651 women aged 19–40 years old who experienced hypertensive disorders during pregnancy; these women had no history of hypertension, diabetes, kidney disease or lupus. We also randomly selected 213 397 women without hypertensive disorders during pregnancy as a comparison cohort; the frequency was matched by age and index year of pregnancy. We compared the incidence of end-stage renal disease in the 2 cohorts. We calculated hazard ratios (HRs) and 95% confidence intervals (CIs) after controlling for demographic and clinical factors.

Results: Women with hypertensive disorders during pregnancy had a greater risk of chronic kidney disease and end-stage renal disease, with adjusted HRs of 9.38 (95% CI 7.09–12.4) and 12.4 (95% CI 8.54–18.0), respectively, after controlling for urban status, coronary artery disease, congestive heart failure, hyperlipidemia and abruption. The HR for end-stage renal disease was 2.72 (95% CI 1.76–4.22) after we also controlled for hypertension and diabetes. Women with preeclampsia or eclampsia had a higher risk of end-stage renal disease (adjusted HR 14.0, 95% CI 9.43–20.7) than women who had gestational hypertension only (adjusted HR 9.03, 95% CI 5.20–15.7).

Interpretation: Women with hypertensive disorders during pregnancy were at a high risk of end-stage renal disease. The risk was much greater for women who had preeclampsia or eclampsia than those who had gestational hypertension only.

Competing interests: None declared.

This article has been peer reviewed.

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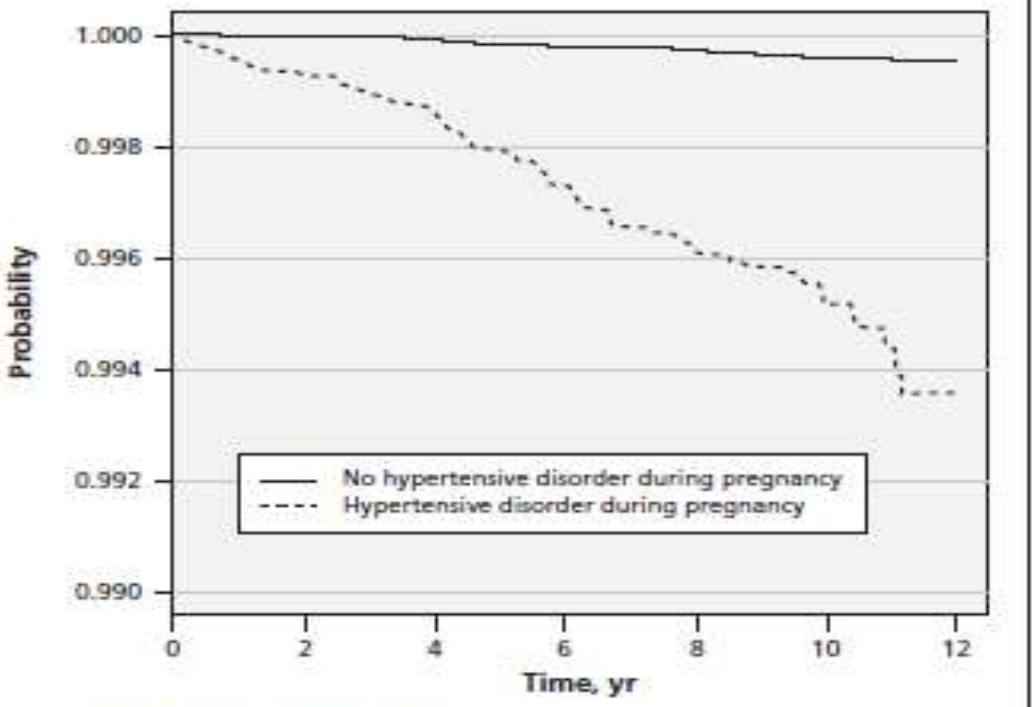
Fung-Chang Sung,
fcsung@mail.cmu.edu.tw

CMAJ 2013. DOI:10.1503/cmaj.120230



No hypertensive disorder during pregnancy						
No. at risk	213 397	179 347	145 072	113 185	82 079	43 202
No. of events	3	11	14	8	7	2
Hypertensive disorder during pregnancy						
No. at risk	26 651	22 377	18 147	14 170	10 231	5 344
No. of events	18	13	22	15	6	5

Figure 1: Estimated proportion of women without end-stage renal disease among those with and without hypertensive disorders during pregnancy. Log-rank test, $p < 0.001$.

CMAJ 2013. DOI:10.1503

Preeclampsia and the Risk of End-Stage Renal Disease

Bjørn Egil Vikse, M.D., Ph.D., Lorentz M. Irgens, M.D., Ph.D., Torbjørn Leivestad, M.D., Ph.D., Rolv Skjærven, Ph.D., and Bjarne M. Iversen, M.D., Ph.D.

ABSTRACT

BACKGROUND

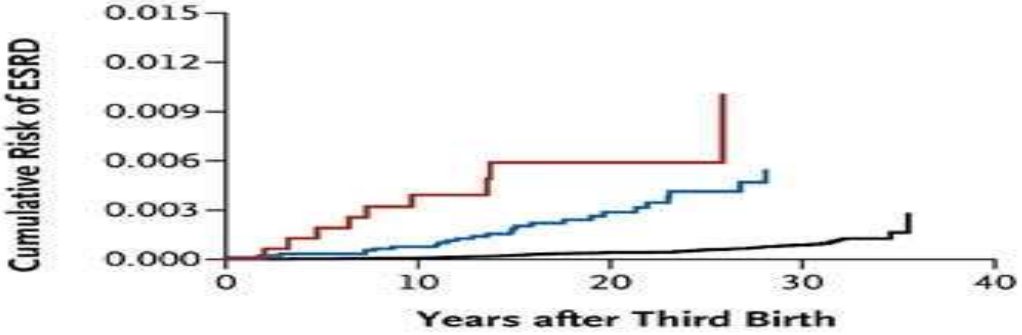
It is unknown whether preeclampsia is a risk marker for subsequent end-stage renal disease (ESRD).

METHODS

We linked data from the Medical Birth Registry of Norway, which contains data on all births in Norway since 1967, with data from the Norwegian Renal Registry, which contains data on all patients receiving a diagnosis of end-stage renal disease (ESRD) since 1980, to assess the association between preeclampsia in one or more pregnancies and the subsequent development of ESRD. The study population consisted of women who had had a first singleton birth between 1967 and 1991; we included data from up to three pregnancies.

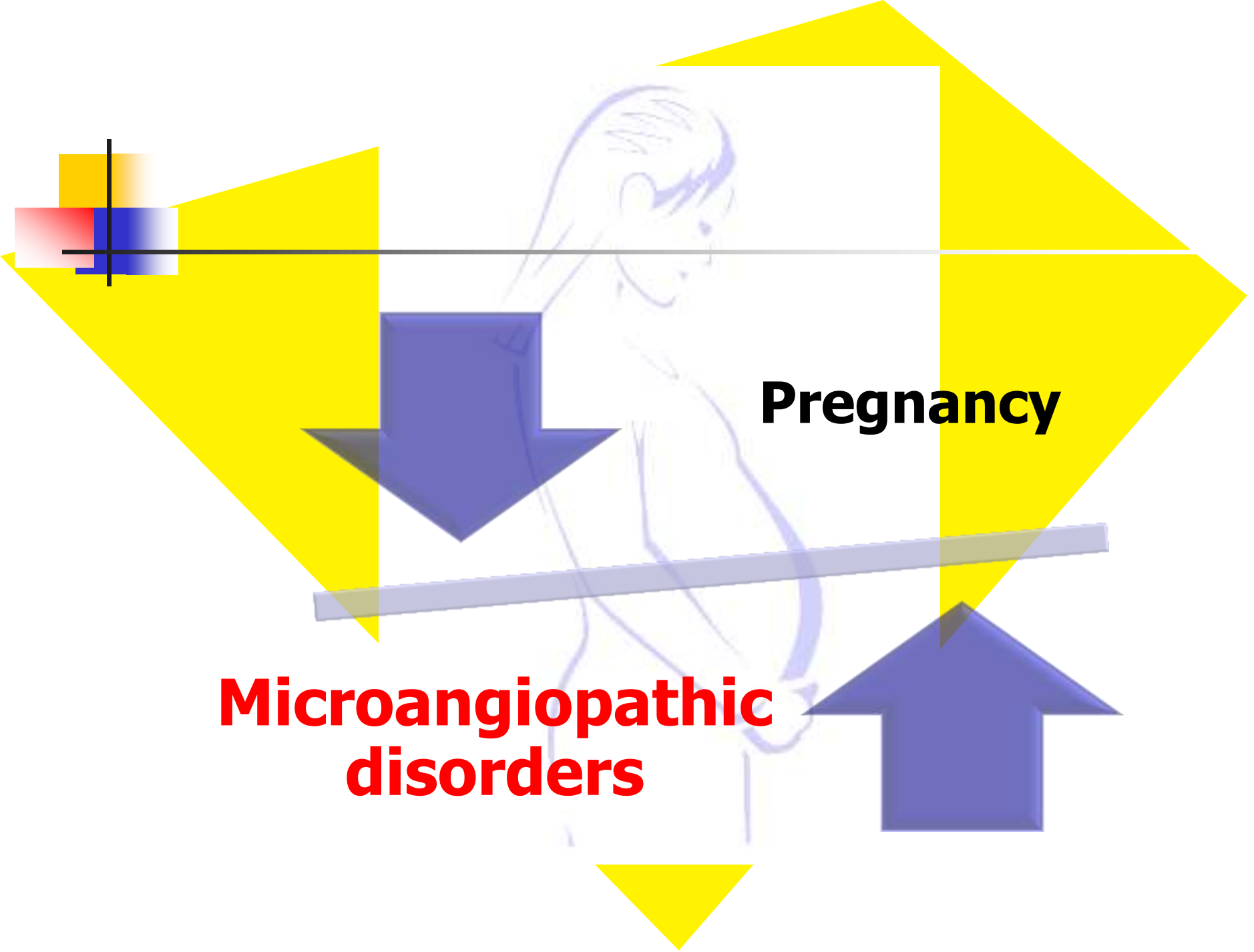
NEJM 2008 Aug 21;359(8):800-9

C After Three Pregnancies



— Preeclampsia in Two or More Pregnancies					
No. at risk	1498	1359	516	102	0
No. with ESRD	0	6	8	9	9
— Preeclampsia in One Pregnancy					
No. at risk	8708	8638	4020	974	0
No. with ESRD	0	7	20	26	26
— No Preeclampsia					
No. at risk	151,346	166,165	86,389	23,000	0
No. with ESRD	0	14	56	76	84

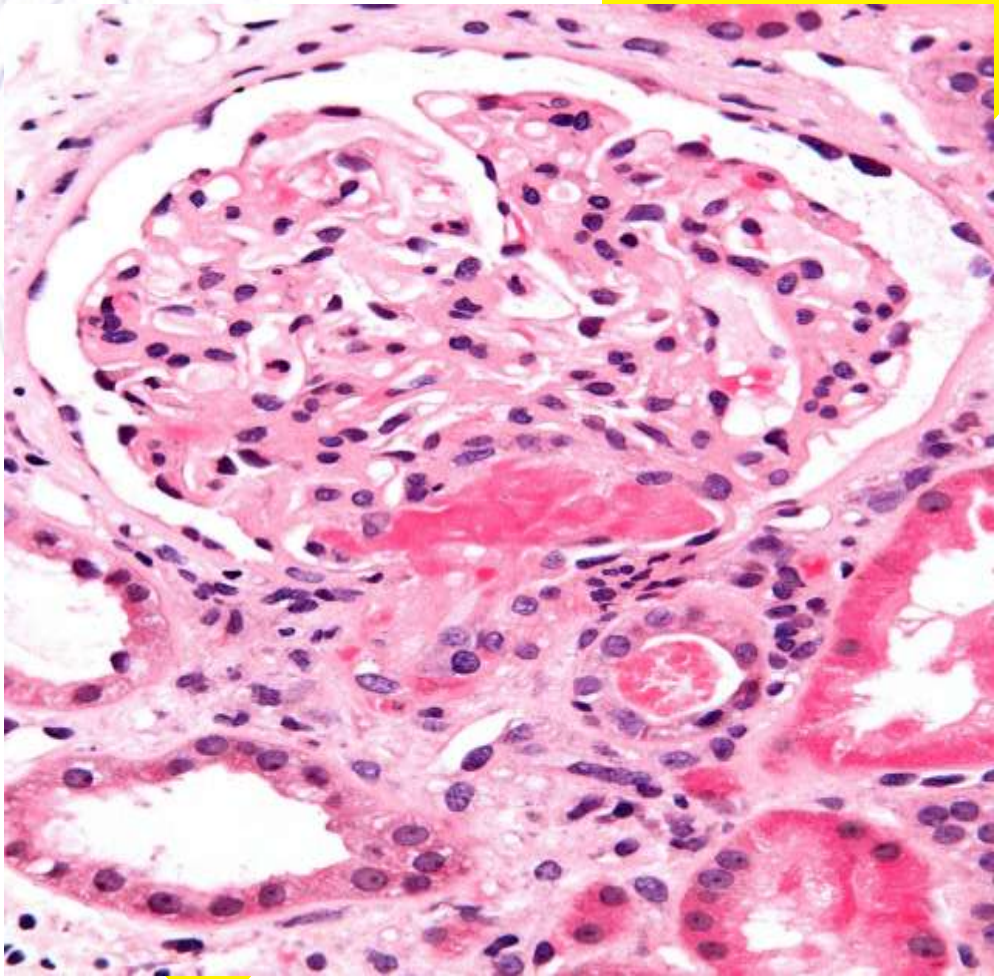
NEJM 2008 Aug 21;359(8):800-9


Pregnancy
Microangiopathic disorders

Microangiopathies in pregnancy

AKI, and share several clinical features which pose diagnostic challenges to the clinician.

- ***HELLP***
- ***AFLP***
- ***TTP***
- ***HUS***
- ***CAPLS***



SciMedCentral

Medical Journal of Obstetrics and Gynecology

Research Article

Pregnancy Associated Thrombotic Microangiopathies Overlap Syndrome: 3 Years Experience at a Tertiary Hospital

Mostafa FG*, Ihab FS, Hassan AB, Wael S and Maha AS

Depetment of Obstetrics and Gynecology, AIN Shams university Cairo, Egypt

*Corresponding authors
Mostafa Fouad Gomaa, Department of Obstetrics and Gynecology, AIN Shams University Cario, Egypt, Tel: 01226188993; Email: Mostafafouadg@gmail.com

Submitted: 15 July 2014

Accepted: 07 August 2014

Published: 09 August 2014

ISSN: 2333-6439

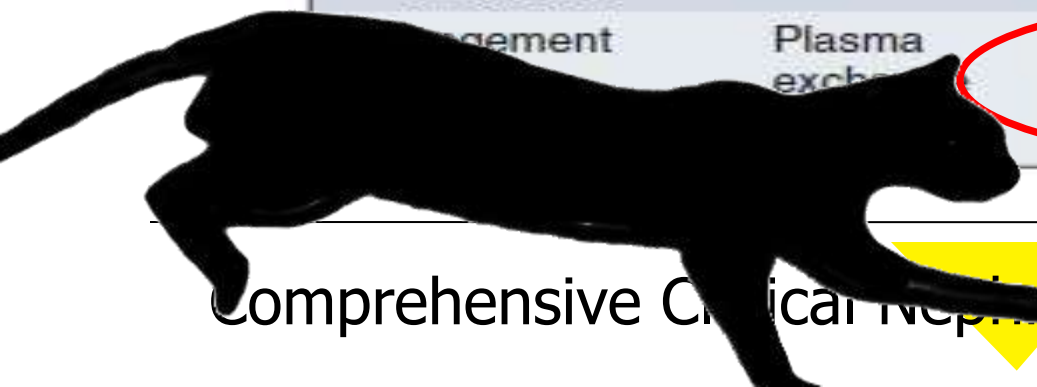
Keywords

- Thrombotic microangiopathies
- AFLP
- HELLP syndrome
- TTP
- HUS

Conclusion: Thrombotic microangiopathies during pregnancy can hardly be differentiated from case of HELLP$, AFLP and ICP. These disorders should be considered a continuum and a spectrum of a single disorder. Early termination of pregnancy with the start of plasma exchange, pulsed steroid therapy and plasmapharesis can result in marked reduction of maternal mortality in such cases.

Comparison of Clinical and Laboratory Characteristics of TTP/HUS, HELLP and AFLP

Clinical Feature	HUS/TTP	HELLP	AFLP
Hemolytic anemia	+++	++	+/–
Thrombocytopenia	+++	++	+/–
Coagulopathy	–	+/–	+
CNS symptoms	++	+/-	+/–
Renal failure	+++	+	++
Hypertension	+/–	+++	+/–
Proteinuria	+/–	++	+/–
Elevated AST	+/–	++	+++
Elevated bilirubin	++	+	+++
Anemia	++	+	+/–
Blood ammonia	Normal	Normal	High
Effect of delivery on disease	None	Recovery	Recovery
gement	Plasma exch	Supportive care, delivery	Supportive care, delivery



Comprehensive Clinical Nephrology, 4th ed,41,567(2010)l

EXTENDED REPORT

Catastrophic antiphospholipid syndrome during pregnancy and puerperium: maternal and fetal characteristics of 15 cases

José A Gómez-Puerta, Ricard Cervera, Gerard Espinosa, Ronald A Asherson, Mario García-Carrasco, Izaias P da Costa, Danieli C O Andrade, Eduardo F Borba, Alexander Makatsaria, Silvia Bucciarelli, Manuel Ramos-Casals, Josep Font, for the Catastrophic Antiphospholipid Syndrome Registry Project Group/European Forum on Antiphospholipid Antibodies*

Ann Rheum Dis 2007;66:740–746. doi: 10.1136/ard.2006.061671

7 of 15 patients had systemic lupus. The CAPS occurred during pregnancy in 8 patients, postpartum in 6 patients and 1 case after curratte of featal death

The kidneys, lungs and brain were the most commonly affected organs

Mortality rate was high for the mothers (46%), and for the babies (54%).

Pregnancy Unrelated Glomeruler Diseases

Glomeruler diseases

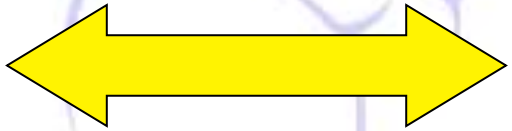
Glomerular disease may be active or quiescent at conception, may flare during pregnancy, or may occur de novo during pregnancy.

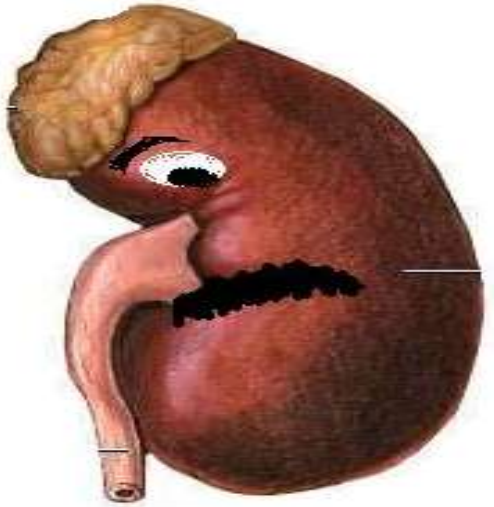
- IgA Nephropathy
- Focal Segmental Glomerulosclerosis
- Minimal Change Disease
- Membranous Nephropathy

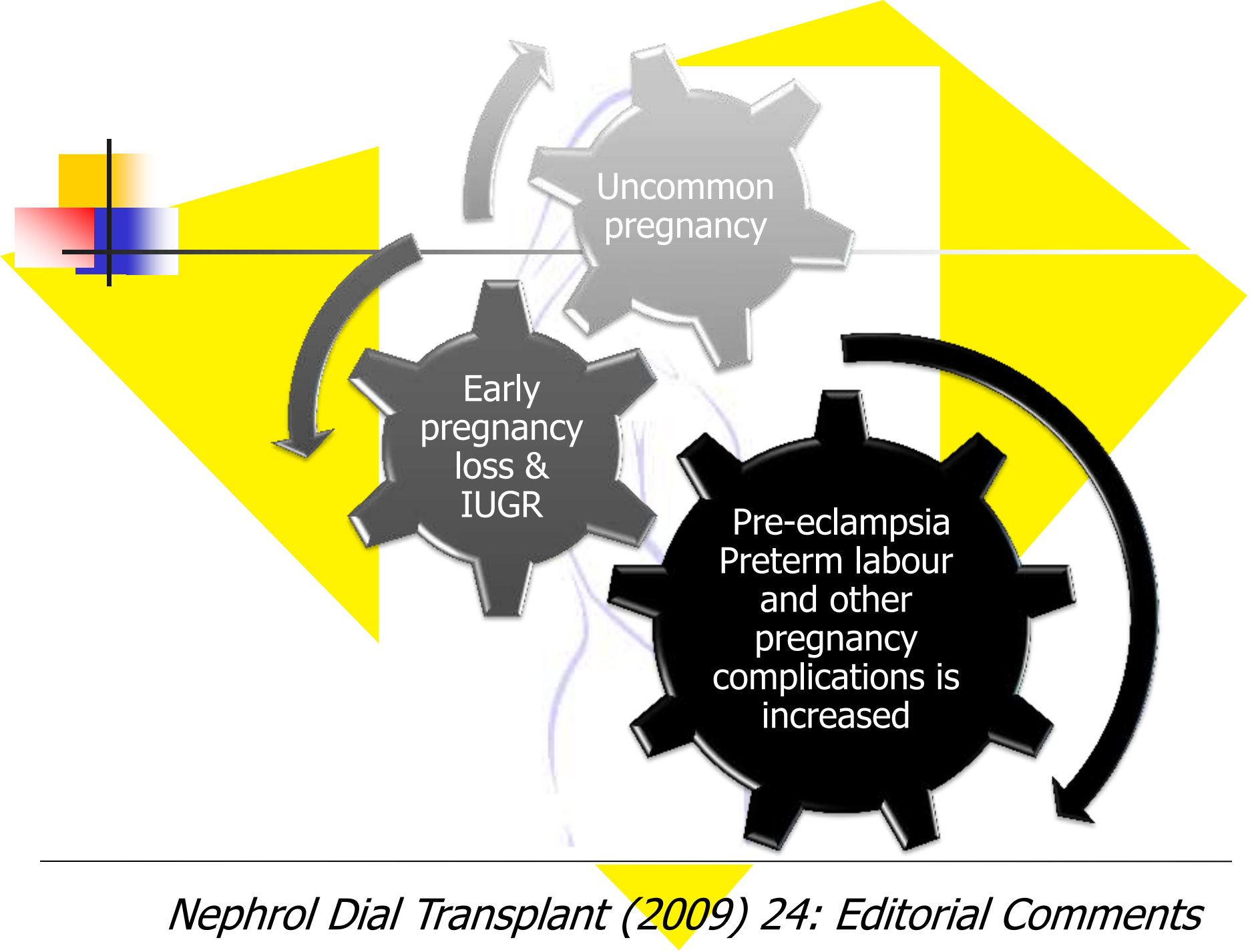
- Diabetic Nephropathy
- Lupus Nephritis
- Systemic Sclerosis/Scleroderma
- Vasculitides

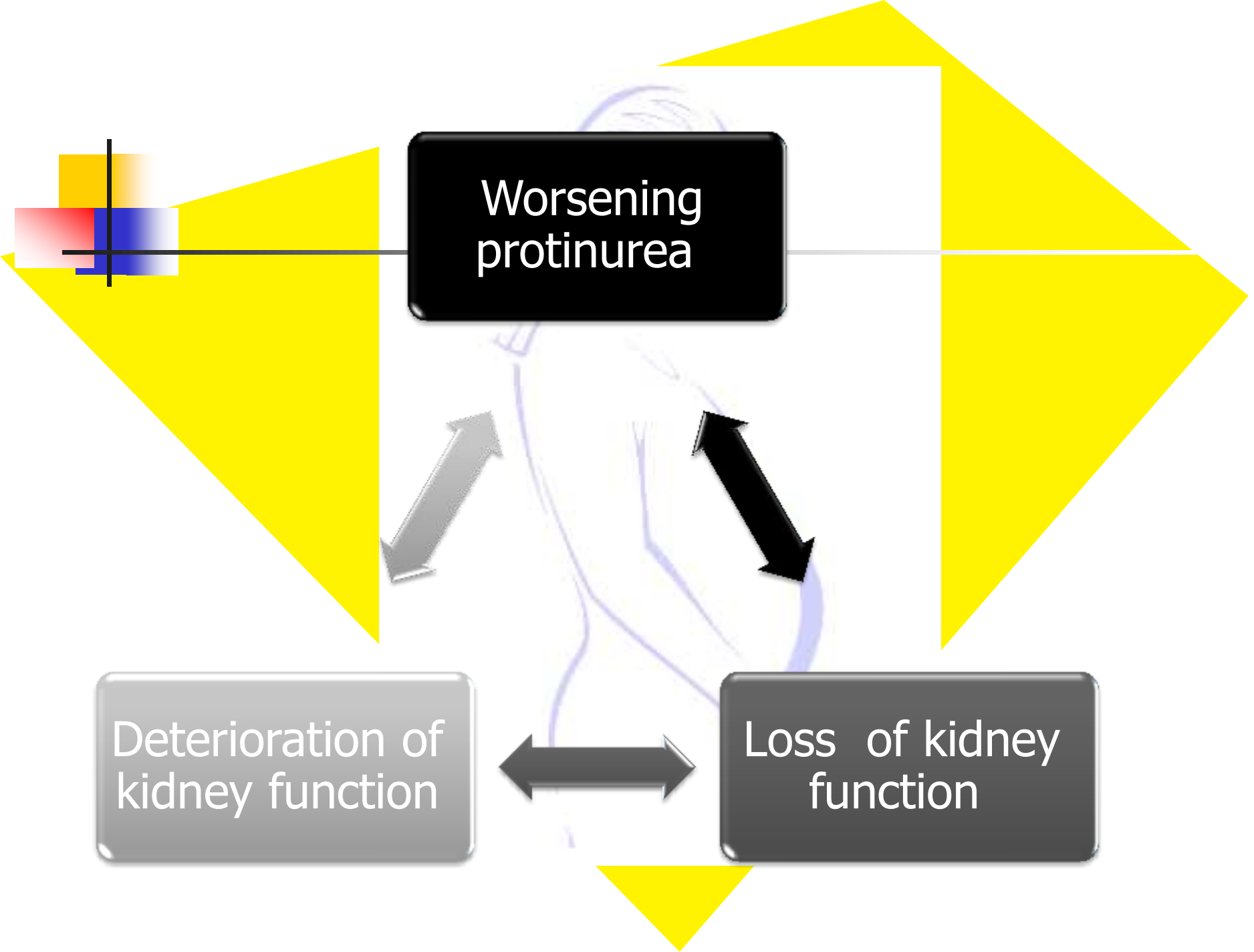
Complex Relationship

* The effects of pregnancy on maternal disease activity and progression
* The impact of the disease and related medical therapy on pregnancy outcome.






Uncommon pregnancy
Early pregnancy loss & IUGR
Pre-eclampsia Preterm labour and other pregnancy complications is increased


Worsening protinurea
Deterioration of kidney function
Loss of kidney function

Factors predicting the outcome

The key pre-pregnancy factors predicting outcome include:

- Degree of renal impairment.
- Control of hypertension before pregnancy.
- Degree of proteinuria.
- Disease activity prior to conception

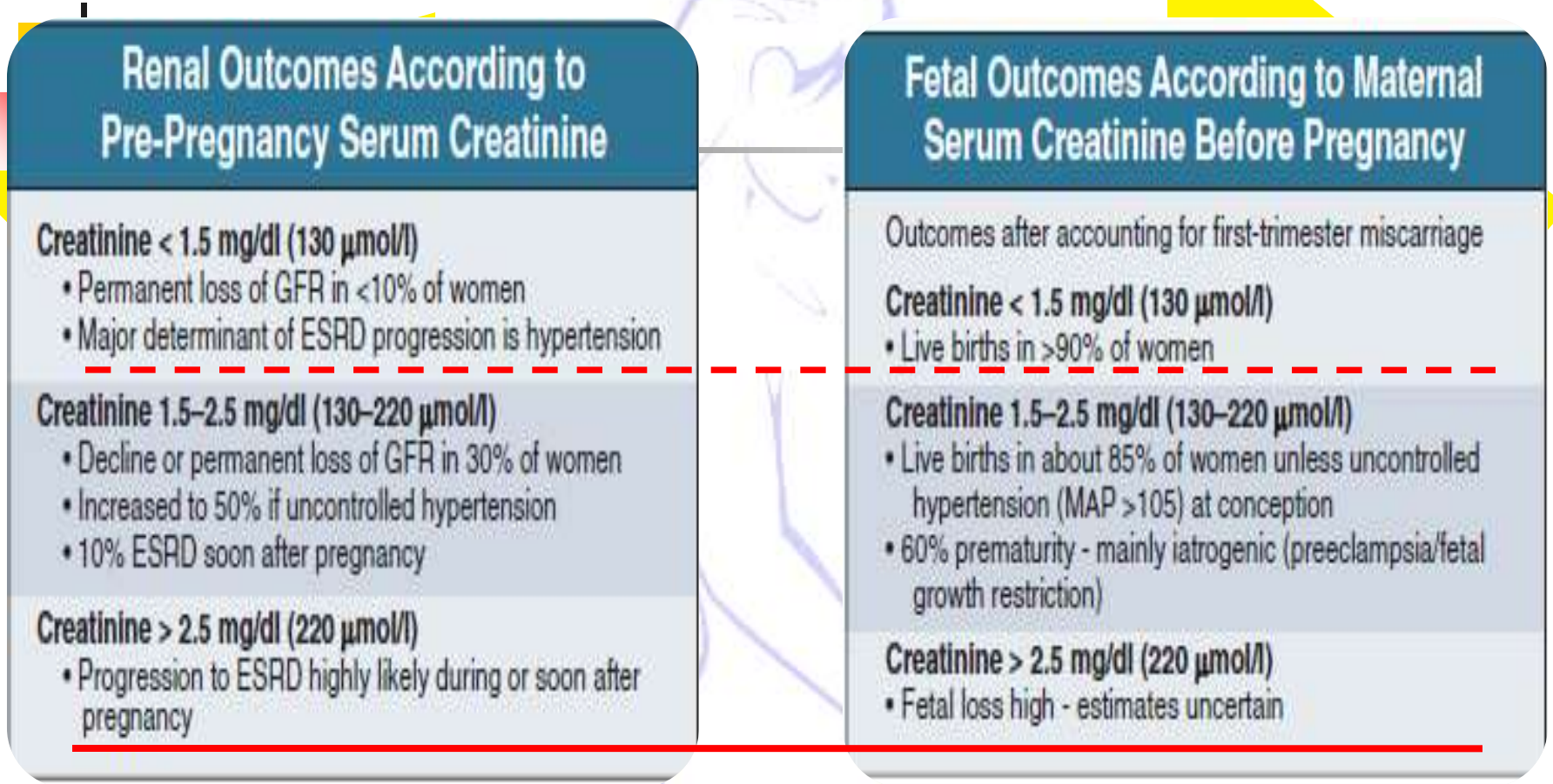
In most of circumstances, these features are more important than the mother's specific renal disease in predicting outcome.

Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.



Comprehensive Clinical Nephrology, 4th ed,41,498(2010)

Mother's specific renal disease

Kidney International, Vol. 30 (1986), pp. 914–919

CLINICAL INVESTIGATION

Successful pregnancy in primary glomerular disease

P. BARCELÓ, J. LÓPEZ–LILLO, L. CABERO, and G. DEL RÍO

Department of Nephrology "Fundación Puigvert" and Department of Obstetrics and Gynecology. Hospital de la Sta, Creu i Sant Pau, Universidad Autónoma, Barcelona, Spain

66 pregnancies in 48 women They were: MPGN in 16 patients, FSGS in 13, IgA nephropathy in 10, MN in 7 and.

Women with membranoproliferative glomerulonephritis appeared to fare worse, and those with IgA nephropathy and membranous nephropathy better than the rest.

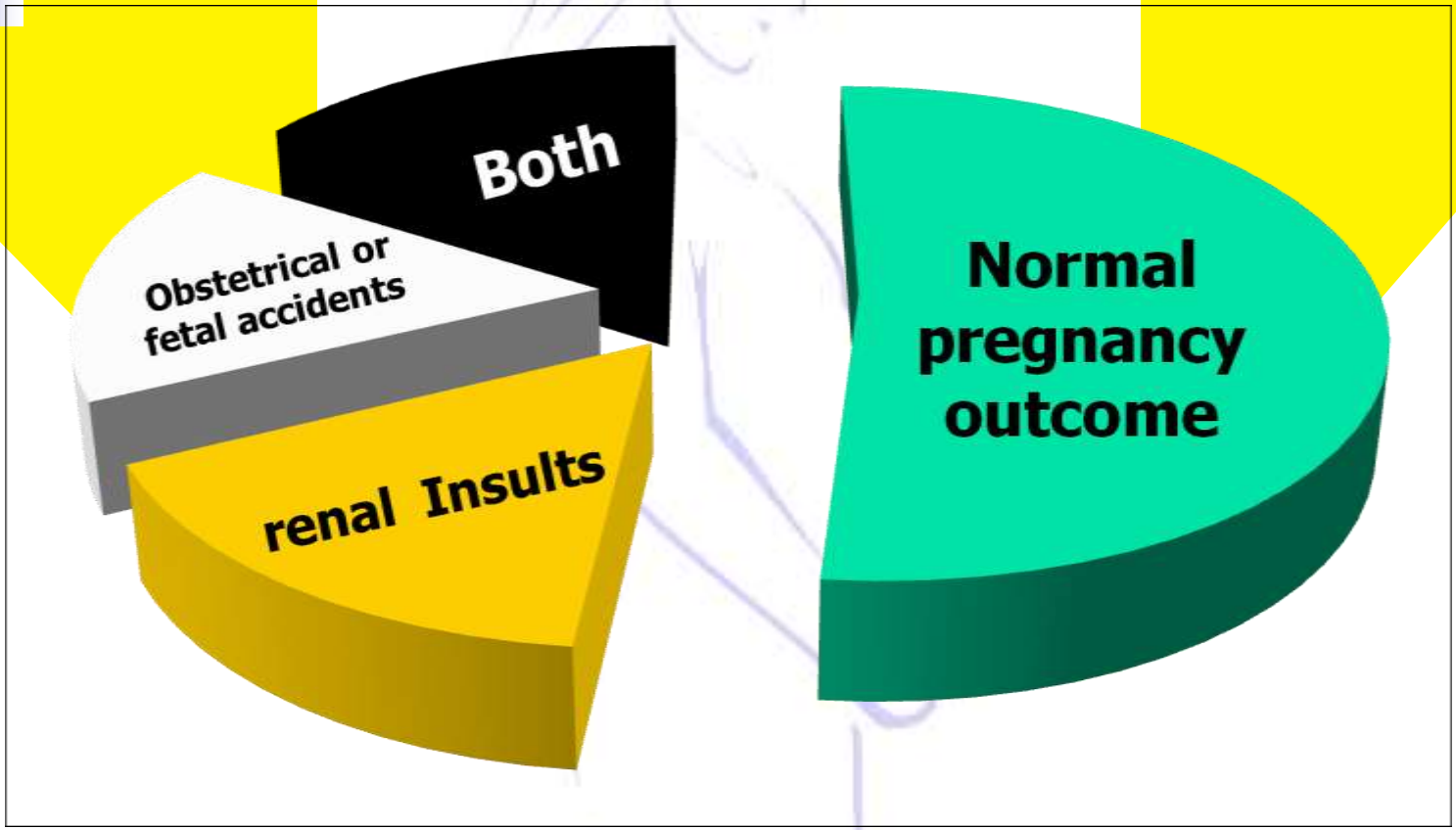
Pregnancy and natural history of glomeruler disease

Glomerular disease and pregnancy. A study of 123 pregnancies in patients with primary and secondary glomerular diseases.

123 pregnancies in 86 patients with biopsy-proven glomerular diseases have been studied. In 35 women the onset of nephropathy occurred during pregnancy.

Nephron: 1984;36(2):101-5.

In most patients with glomeruler D …, pregnancy does not change its natural history



Renal function deteriorated in 10 of 86 cases during pregnancy. The deterioration was reversible in 6 and progressive in 4..

PREGNANCY IN DIABETES AND KIDNEY DISEASE

Kate Bramham[1], MRCP, Daghni Rajasingham[2], FRCOG
[1]Maternal and Fetal Research Unit, King's College London, London, UK
[2]Department of Obstetrics and Gynaecology, Guy's and St. Thomas' NHS Foundation Trust, London, UK

Bramham K., Rajasingham D. (2012). Pregnancy in diabetes and kidney disease. *Journal of Renal Care* 38(Suppl. 1), 78-89.

SUMMARY

With appropriate multi-disciplinary team care, most women with diabetic nephropathy will have successful pregnancy outcomes; however, pregnancy complications are increased compared to non-diabetic individuals, particularly in those with poor glycaemic control. Women with more severe renal impairment, especially those with hypertension and proteinuria at are highest risk of worse pregnancy outcomes and deterioration in pre-existing renal function. Pre-pregnancy counselling should be offered to all women with diabetes in order to optimise diabetic care, and inform women of potential complications. Pregnancy is an indicator of long-term health, and may indicate important issues for the future management of women with diabetic nephropathy.

I am a Lupus pt.....
Can I still plan a pregnancy?

12.11: Systemic lupus and pregnancy

12.11.1: We suggest that women be counseled to delay pregnancy until a complete remission of LN has been achieved. *(2D)*

NIH Public Access
Author Manuscript
Lupus. Author manuscript; available in PMC 2009 August 11.

Published in final edited form as:
Lupus. 2009 April ; 18(4): 342–347. doi:10.1177/0961203308097575.

Maternal and Fetal Outcomes in Pregnant Patients with Active Lupus Nephritis

58 patients with LN (A&Q) are Compared to 47 lupus patients without LN.

Pregnancies in patients with active lupus nephritis were associated with a higher incidence of maternal complications (57% vs. 11%), rather than quiescent lupus nephritis . (35% vs. 11%)


Responsibility

CMAJ COMMENTARY

Can we protect the kidneys after hypertensive pregnancy?

Julia J. Spaan MD PhD, Mark A. Brown MD

KEY POINTS

- There is an increased risk of end-stage renal disease among women with a history of preeclampsia; those with the more benign disorder of gestational hypertension alone are also at increased risk.
- The development of hypertension, diabetes or both after pregnancy is an important mediator of chronic kidney disease.
- Blood pressure should be monitored regularly after a hypertensive disorder during pregnancy.
- Cardiovascular risk management in a structured multidisciplinary approach may reduce cardiovascular and renal disease after a hypertensive disorder during pregnancy.

CMAJ 2013. DOI:10.1503

Multidisiplinary Team

Thank You